REMARKS

Claims 73, 74, 76, 78, 80-82, 86-89 and 92-103 are pending in the instant application. Claims 81 and 88 have been withdrawn from consideration by the Examiner. Claims 73, 74, 76, 78, 80, 82, 86-87, 89 and 92-103 have been rejected. Claim 73 has been amended. No new matter has been added by the amendments. Reconsideration is respectfully requested in light of the amendments and the following remarks.

I. Species Election

Claims 73, 74, 76, 78, 80-82, 86-89 and 92-103 are pending in the instant application. The Examiner has withdrawn claim 81 and 88 suggesting that these claims do not read on the elected species. In accordance with MPEP § 809.01 and 37 C.F.R. § 1.146, it is respectfully pointed out that the claims should only be restricted to the elected species if no generic claim is held allowable. Accordingly, upon allowance of the generic claims, it is respectfully requested that claims 81 and 88 be rejoined.

II. Rejection of Claims 73, 74, 76, 78, 80, 82, 86-87 and 92-103 under 35 U.S.C. 112, second paragraph

Claims 73, 74, 78, 80, 82, 86-87, 89 and 92-103 have been

rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner suggests that it is unclear in step (c) what is meant by "free thiol". Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended step (c) to clarify that the thiol product is converted active thiol product from step (b).

Withdrawal of this rejection is respectfully requested.

III. Rejection of Claims 73, 74, 76, 78, 80, 82, 86-87, 89 and 92-103 under 35 U.S.C. 112, first paragraph - Written Description

Claims 73, 74, 78, 80, 82, 86-87, 89 and 92-103 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner suggests that claims 73 and 86 recite "a compound which reduces active thiol(s)" while the specification only describes DTNB.

Applicants respectfully traverse this rejection.

Applicants respectfully disagree with the Examiner's suggestion that "the specification only describes DTNB." The

phrase "compound which reduces active thiol(s)" is used throughout the specification at, for example, page 10, lines 17-18 and lines 22-23, page 18, lines 25-26 and page 20, line 4. Further, the phrase "compound which reduces active thiol(s)" was part of the original claim set.

Quite clear from use of the phrase "compound which reduces active thiol(s)" in the instant specification is that at the time of the invention Applicants contemplated use of compounds other than DTNB to reduce active thiol(s) in the method of the instant invention.

The Examiner's suggestion that "the specification only describes DTNB" appears to be based upon the working example which uses DTNB as the compound to reduce active thiols. It is respectfully pointed out that such basis is improper. The Court of Appeals for the Federal Circuit has explained that, "(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met … even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." *Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 USPQ2d 1001, 1007

(Fed. Cir. 2006). See also *Capon v. Eshhar*, 418 F.3d at 1358, 76 USPQ2d at 1084 ("The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes" where the genes were novel combinations of known DNA segments.). Also see MPEP 2163.

Further, the Courts have recognized that there are situations where one species adequately supports a genus. See, e.g., *Rasmussen*, 650 F.2d at 1214, 211 USPQ at 326-27 (disclosure of a single method of adheringly applying one layer to another was sufficient to support a generic claim to "adheringly applying" because one skilled in the art reading the specification would understand that it is unimportant how the layers are adhered, so long as they are adhered); *In re Herschler*, 591 F.2d 693, 697, 200 USPQ 711, 714 (CCPA 1979) (disclosure of corticosteroid in DMSO sufficient to support claims drawn to a method of using a mixture of a "physiologically active steroid" and DMSO because "use of known chemical compounds in a manner auxiliary to the invention must have a corresponding written description only so specific as to lead one having ordinary skill in the art to that class of compounds." Also see

MPEP 2163.

Similar to the invention in Rasmussen, in the instant invention it is unimportant in step (a) how active thiol(s) in the sample is reduced, so long as it is reduced. Those skilled in the art reading the instant specification, which expressly discloses using a compound which reduces active thiol(s), would under this.

Further, similar to the facts in Herschler, Applicants are using known chemical compounds in a manner auxiliary to the invention and have provided a written description which would lead one having ordinary skill in the art to that class of compounds. The Examiner has acknowledged that other thiol reducing agents are well-known. See page 6 of the Office Action mailed February 8, 2010 and page 3 of the Final Rejection mailed September 9, 2010. In addition, the instant specification expressly discloses as a class compounds which reduce active thiol(s).

Accordingly, the case law makes clear that the instant specification meets the written description requirements for the instant claimed invention.

Also clear is MPEP 2163 which states that a description as filed is presumed to be adequate, unless or until sufficient

evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. See, e.g., *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description. The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *Wertheim*, 541 F.2d at 263, 191 USPQ at 97. In rejecting a claim, the examiner must set forth express findings of fact regarding the above analysis which support the lack of written description conclusion.

It is respectfully submitted that the Examiner has failed to meet this burden as no facts or evidence have been set forth supportive of a lack of written description conclusion with respect to the phrase "compounds which reduce active thiol(s)." Instead, the Examiner has acknowledged that other thiol reducing agents such as DTT and mercaptoethanol are known.

In contrast, Applicants have specifically pointed to areas of the originally filed specification wherein the phrase "compounds which reduce active thiol(s)." This phrase was also part of the original claims. In addition, it has been

acknowledged that other thiol reducing agents are known. The evidence of record, when viewed as a whole, is thus clearly supportive of the specification meeting the written description requirements of 35 U.S.C. 112, first paragraph.

Withdrawal of this rejection is therefore respectfully requested.

IV. Rejection of Claims under 35 U.S.C. 103(a)

Claims 73, 74, 76, 78, 80, 82 and 92 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Farooqui et al. (J. Lipid. Res. 1984) in view of Murata et al. (Chem. Phar. Biol. 1991).

Claims 93-98 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Farooqui et al. (J. Lipid. Res. 1984) in view of Murata et al. (Chem. Phar. Biol. 1991) as described above and further in view of Benitez et al. (Circulation 2003).

Claims 86, 87, 89 and 99-103 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Farooqui et al. in view of Murata et al. as described above and further in view of Maret et al. (U.S. Patent 5,478,741). Maret is cited for its teaching of putting assay components in a kit.

Applicants respectfully traverse this rejection.

Applicants respectfully disagree with the Examiner's characterization of the teachings of Farooqui et al.

Contrary to the Examiner's suggestion, page 1557: line 27 of left column to line 33 of right column and Figure 2 of Farooqui et al. do not disclose "a method for measuring enzymatically activity phospholipases". Instead, teachings at page 1557 and Figure 2 are related to monoacylglycerol lipase and diacylglycerol lipase. See Header I in col. 1 of page 1557 "Monoacylglycerol lipase": Header II in col. 2 of page 1557 "Diacylglycerol lipase"; and Fig. 2. entitled "Action of diacylglycerol lipase on the thioester substrate analog and the reaction of DTNB with sulfhydryl group." Accordingly, the teachings of Farooqui et al. at page 1557 relied upon the Examiner are in no way predictive of the instant claimed assay for a completely different enzyme, namely Lipoprotein-associated Phospholipase A2.

At page 1559 of Farooqui et al., a method for determining phospholipase A2 activity is disclosed. See Header II in col. 1 of page 1559 "Determination of phospholipase A_2 activity" as well as page 1559 col. 2 in the first full paragraph. However, for the phospholipase A2 assay, Farooqui et al. do not teach incubating the sample with a compound which reduces active

thiol(s) in the sample for a time sufficient for said compound to reduce said active thiol(s) prior to contacting the incubated sample with a substrate that is converted to an active thiol product by enzymatically active Lp-PLA2. Accordingly, the teachings of Farooqui et al. for measuring activity of phospholipase A2, a molecule more closely related to Lipoprotein-associated Phospholipase A2, are in no way predictive of the instant claimed assay and do not teach or suggest all limitations of the instant claimed assay.

Further, Applicants note for clarity that while a phospholipase A2 assay is taught by Farooqui et al., it is a completely different enzyme from Lipoprotein-associated Phospholipase A2. For example, Farooqui et al. teach at page 1559 col. 2 that "…[phospholipase A2] has an absolute requirement for Ca^{2+}, while the instant application teaches at page 1 that Lp-PLA2 is Ca^{2+} independent. Therefore, while the phospholipase A2 taught by Farooqui et al. and Lp-pLA2 of the instant invention are both members of the phospholipase A2 family of enzymes, they are completely different enzymes and the method for determining phospholipase A2 taught by Farooqui et al., which actually differs from the instant claimed invention in both steps and enzymatic activity measured, is in no way predictive of the

instant claimed assay.

Secondary references of Murata et al. (Chem. Phar. Biol. 1991), Benitez et al. (Circulation 2003), and Maret et al. (U.S. Patent 5,478,741) fail to remedy deficiencies in the primary reference of Farooqui et al. as these secondary references are also not predictive of the instant claimed assay for Lipoprotein-associated Phospholipase A2 and fail to teach or suggest all limitations of the instant claimed assay.

Thus, as the cited combinations of references fail to provide the required reasonable expectation of success with respect to the instant claimed invention and do not teach or suggest all limitations of the instant claimed assay, they cannot render obvious the instant claimed assay. See MPEP 2143.01 and 2143.02.

Withdrawal of these rejections under 35 U.S.C. 103(a) is therefore respectfully requested.

V. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending

claims is earnestly solicited.

Respectfully submitted,

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